09622815

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 19	APOLLIT offering free connect time in April 2003
NEWS 28	Mar 20	EVENTLINE will be removed from STN
NEWS 29	Mar 24	PATDPAFULL now available on STN
NEWS 30	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 31	Apr 11	Display formats in DGENE enhanced
NEWS 32	Apr 14	MEDLINE Reload
NEWS 33	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 34	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 35	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 36	Apr 28	RDISCLOSURE now available on STN
NEWS 37	May 05	Pharmacokinetic information and systematic chemical names added to PHAR

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 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 10:18:24 ON 10 MAY 2003

=> fil reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:18:32 ON 10 MAY 2003
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:    9 MAY 2003  HIGHEST RN 513416-44-9
DICTIONARY FILE UPDATES:   9 MAY 2003  HIGHEST RN 513416-44-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09622815.str

L1      STRUCTURE UPLOADED

=> d
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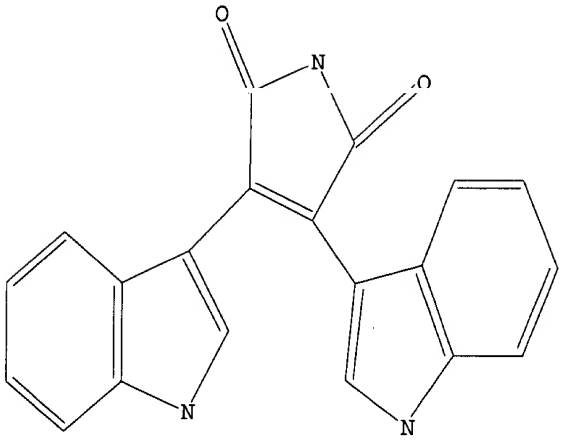
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam
SAMPLE SEARCH INITIATED 10:18:53 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 89 TO ITERATE

100.0% PROCESSED 89 ITERATIONS 50 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1214 TO 2346
PROJECTED ANSWERS: 576 TO 1424

L2 50 SEA SSS SAM L1

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.40	0.61

FILE 'CAPLUS' ENTERED AT 10:19:01 ON 10 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

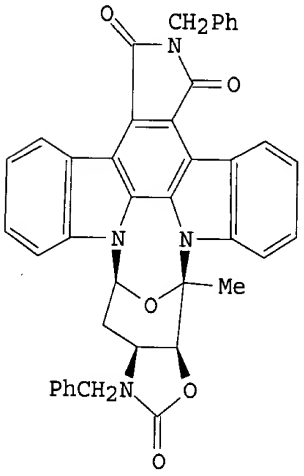
FILE COVERS 1907 - 10 May 2003 VOL 138 ISS 20
FILE LAST UPDATED: 9 May 2003 (20030509/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2 full
L3 75 L2

=> d l3 65-75 ibib abs hitstr

L3 ANSWER 65 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:428486 CAPLUS
DOCUMENT NUMBER: 119:28486
TITLE: The first synthesis of a fully functionalized core structure of staurosporine: sequential indolyl glycosidation by endo and exo glycals
AUTHOR(S): Link, J. T.; Gallant, Michel; Danishefsky, Samuel J.; Huber, Susan
CORPORATE SOURCE: Dep. Chem., Yale Univ., New Haven, CT, 06511-8118, USA
SOURCE: Journal of the American Chemical Society (1993), 115(9), 3782-3
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The first synthesis of a fully functionalized core structure, i.e. I, of staurosporine is described. The route relies upon a novel intramol. indolyl glycosidation of an exo glycal to give the ring system.

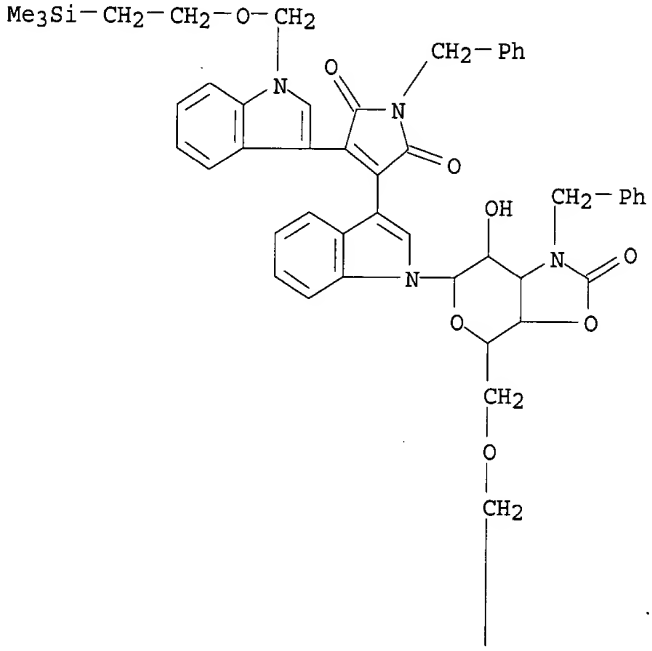
IT **148301-99-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 148301-99-9 CAPLUS

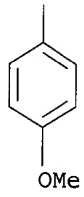
CN 1H-Pyrrole-2,5-dione, 3-[1-[hexahydro-7-hydroxy-4-[[(4-methoxyphenyl)methoxy]methyl]-2-oxo-1-(phenylmethyl)-2H-pyrano[4,3-d]oxazol-6-yl]-1H-indol-3-yl]-1-(phenylmethyl)-4-[1-[[2-

(trimethylsilyl)ethoxy]methyl]-1H-indol-3-yl]-, [3aS-(3a.alpha.,4.alpha.,6.alpha.,7.beta.,7a.alpha.)]- (9CI) (CA INDEX NAME)

PAGE 1-A



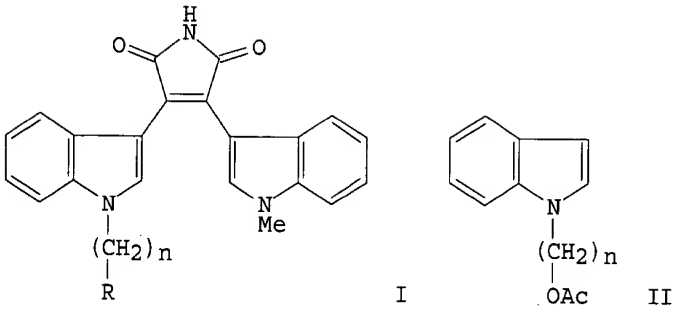
PAGE 2-A



L3 ANSWER 66 OF 75 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1992:448257 CAPLUS
DOCUMENT NUMBER:	117:48257
TITLE:	Inhibitors of protein kinase C. 2. Substituted bisindolylmaleimides with improved potency and selectivity
AUTHOR(S):	Davis, Peter D.; Elliott, Lucy H.; Harris, William; Hill, Christopher H.; Hurst, Steven A.; Keech, Elizabeth; Kumar, M. K. Hari; Lawton, Geoffrey; Nixon, John S.; Wilkinson, Sandra E.
CORPORATE SOURCE:	Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY, UK
SOURCE:	Journal of Medicinal Chemistry (1992), 35(6), 994-1001 CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

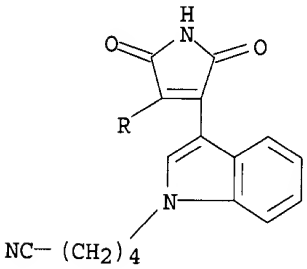
II

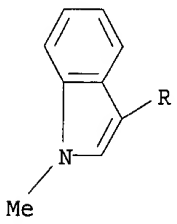
AB Bisindolylmaleimides I [R = OH, NH2, SC(:NH)NH2, n = 2-5; R = NHMe, NMe2, N+Me3, NHC(:NNO2)NH2, NHC(:NH)NH2, CH2C(:NH)NH2, n = 3] were prepd. and their inhibition of protein kinase C was measured. Thus, indole reacted with Br(CH2)nOAc (n = 3-5) or ethylene oxide and Ac2O to give (acetoxyalkyl)indoles II. II condensed with N-methyl-3-indoleacetic acid and NH3 to give I (R = OH, n = 2-5). I [R = SC(:NH)NH2, n = 3] was the most potent inhibitor. Structure activity relationships were consistent with the interaction of a cationic group in the inhibitor with a carboxylate group in the enzyme.

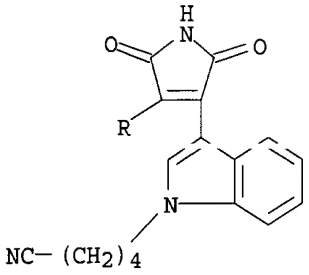
IT **125314-73-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amination of)

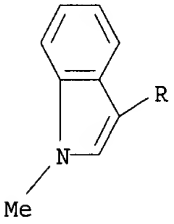
RN 125314-73-0 CAPLUS

CN 1H-Indole-1-pentanenitrile, 3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]- (9CI) (CA INDEX NAME)





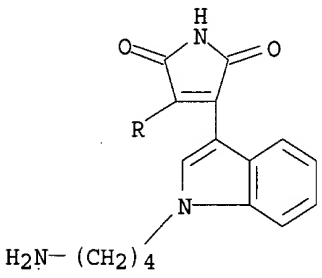


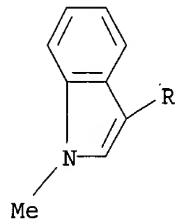


IT **138489-11-9P 138489-17-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and protein kinase C inhibitory activity of)
RN 138489-11-9 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-[1-(4-aminobutyl)-1H-indol-3-yl]-4-(1-methyl-1H-indol-3-yl)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

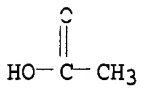
CRN 138489-10-8
CMF C25 H24 N4 O2





CM 2

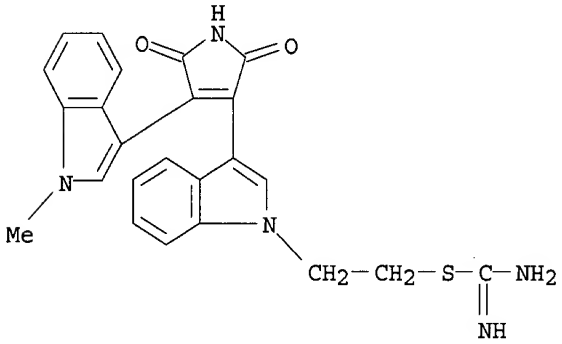
CRN 64-19-7
CMF C2 H4 O2



RN 138489-17-5 CAPLUS
CN Carbamimidothioic acid, 2-[3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]ethyl ester, monomethanesulfonate (9CI) (CA INDEX NAME)

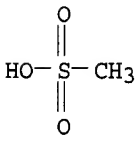
CM 1

CRN 125314-66-1
CMF C24 H21 N5 O2 S



CM 2

CRN 75-75-2
CMF C H4 O3 S

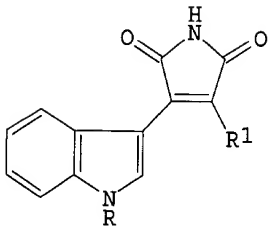


L3 ANSWER 67 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:41230 CAPLUS
DOCUMENT NUMBER: 116:41230
TITLE: Inhibitors of protein kinase C. 1. 2,3-bisarylmaleimides
AUTHOR(S): Davis, Peter D.; Hill, Christopher H.; Lawton, Geoffrey; Nixon, John S.; Wilkinson, Sandra E.; Hurst, Steven A.; Keech, Elizabeth; Turner, Susan E.
CORPORATE SOURCE: Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY,

09622815

	UK
SOURCE:	Journal of Medicinal Chemistry (1992), 35(1), 177-84 CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:	Journal
LANGUAGE:	English

GI



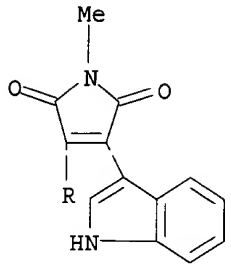
I

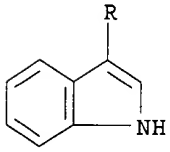
AB A series of novel inhibitors, i.e., maleimides I (R = H, Me; R1 = (un)substituted indolyl, (un)substituted Ph, naphthyl, benzo[b]thien-3-yl, benzo[b]furan-3-yl, 3-pyrrolyl) of protein kinase C (PKC) is described. These maleimides were derived from the structural lead provided by the indolocarbazoles, staurosporine and K252a. Optimum activity required the imide NH, both carbonyl groups, and the olefinic bond of the maleimide ring. Bisindolylmaleimides were the most active and the potency of these was improved by a chloro substituent at the 5-position of one indole ring (IC50 0.11 .mu.M). In a series of (phenylindolyl)maleimides, nitro deriv. I (R = Me, R1 = 2-O2NC6H5) was most active (IC50 0.67 .mu.M). Naphthalene compd. I (R = Me, R1 = 1-naphthyl) and benzothiphene compd. I (R = Me, R2 = benzo[b]thien-3-yl) showed greater than 100-fold selectivity for inhibition of PKC over the closely related cAMP-dependent protein kinase.

IT **113963-68-1P 125313-48-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and protein kinase C inhibiting activity of)

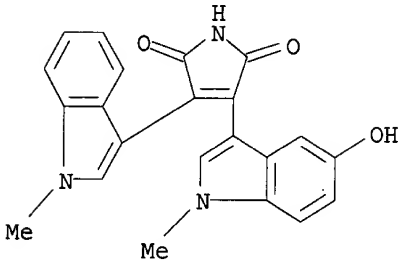
RN 113963-68-1 CAPLUS

CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





RN 125313-48-6 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-(5-hydroxy-1-methyl-1H-indol-3-yl)-4-(1-methyl-1H-indol-3-yl)- (9CI) (CA INDEX NAME)



L3 ANSWER 68 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:674290 CAPLUS
DOCUMENT NUMBER: 115:274290
TITLE: The bisindolylmaleimide GF 109203X is a potent and selective inhibitor of protein kinase C
AUTHOR(S): Toullec, Dominique; Pianetti, Pascal; Coste, Herve; Bellevergue, Patrice; Grand-Perret, Thierry; Ajakane, Myriam; Baudet, Valerie; Boissin, Patrick; Boursier, Eric; et al.
CORPORATE SOURCE: Cent. Rech., Lab. Glaxo, Les Ulis, 91951, Fr.
SOURCE: Journal of Biological Chemistry (1991), 266(24), 15771-81
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

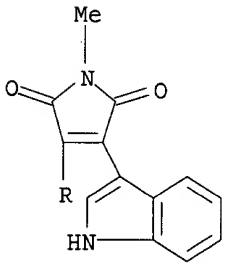
AB Staurosporine is the most potent inhibitor of protein kinase C (PKC) described in the literature with a half-maximal inhibitory concn. (IC50) of 10 nM. Nevertheless, this natural product is poorly selective when assayed against other protein kinases. To obtain specific PKC inhibitors, a series of bisindolylmaleimides has been synthesized. Structure-activity relationship studies allowed the detn. of the substructure responsible for

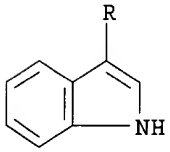
conferring high potency and lack of selectivity in the staurosporine mol. Several aminoalkyl bisindolylmaleimides were found to be potent and selective PKC inhibitors (IC50 values from 5 to 70 nM). Among these compds. GF 109203X has been chosen for further studies aiming at the characterization of this chem. family. GF 109203X was a competitive inhibitor with respect to ATP (Ki = 14 nM) and displayed high selectivity for PKC as compared to five different protein kinases. The potency and specificity of GF 109203X was further detd. in 2 cellular models: human platelets and Swiss 3T3 fibroblasts. GF 109203X efficiently prevented PKC-mediated phosphorylations of an Mr = 47,000 protein in platelets and of an Mr = 80,000 protein in Swiss 3T3 cells. In contrast, in the same models, the PKC inhibitor failed to prevent PKC-independent phoshorylations. GF 109203X inhibited collagen- and .alpha.-thrombin-induced platelet aggregation as well as collagen-triggered ATP secretion. However, ADP-dependent reversible aggregation was not modified. In Swiss 3T3 fibroblasts, GF 109203X reversed the inhibition of EGF binding induced by phorbol 12,13-dibutyrate and prevented [3H]thymidine incorporation into DNA, only when this was elicited by growth promoting agents which activate PKC. These results illustrate the potential of GF 109203X as a tool for studying the involvement of PKC in signal transduction pathways.

IT **113963-68-1**
RL: BIOL (Biological study)
(protein kinase C of human and lab. animal inhibition by and reactions of, structure in relation to)

RN 113963-68-1 CAPLUS

CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)

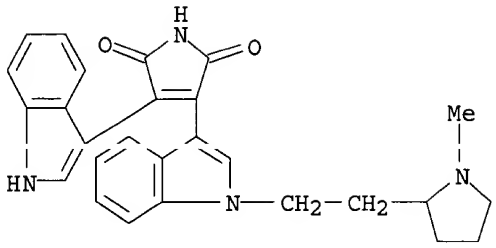




IT **137592-45-1**
RL: BIOL (Biological study)
(protein kinase C of human and lab. animal inhibition by, structure in relation to)

RN 137592-45-1 CAPLUS

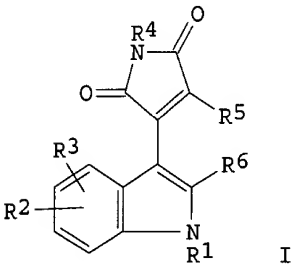
CN 1H-Pyrrole-2,5-dione, 3-(1H-indol-3-yl)-4-[1-[2-(1-methyl-2-pyrrolidinyl)ethyl]-1H-indol-3-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 69 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:632077 CAPLUS
DOCUMENT NUMBER: 115:232077
TITLE: Preparation of bis(indolyl)maleimides and analogs as antiallergics and for use in immune diseases
INVENTOR(S): Tsaklakidis, Christos; Schultz, Michael; Haag, Rainer; Scheuer, Werner; Russmann, Eberhard
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4005969	A1	19910829	DE 1990-4005969	19900226
WO 9113071	A1	19910905	WO 1991-EP330	19910222
W: AU, CA, FI, HU, JP, KR, NO, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9173011	A1	19910918	AU 1991-73011	19910222
PRIORITY APPLN. INFO.:			DE 1990-4005969	19900226
			WO 1991-EP330	19910222

OTHER SOURCE(S): MARPAT 115:232077
GI



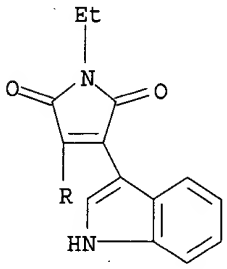
I

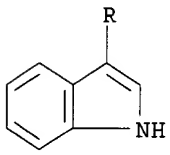
AB The title compds. [I; R1 = H, (acyl)carbohydrate residue, (un)substituted (un)satd. aliph. group; R2, R3 = H, halo, alkyl, OH, etc.; R4 = cyano, C(:NH)NH2, (un)substituted cycloalkyl, (hetero)aryl, etc.; R5 = (hetero)aryl; R6 = H, carbalkyl, aryl, (un)substituted aminoalkyl, etc.] were prepd. as antiallergics and for use in immune disorders (no data). Thus, 3,4-bis(3-indolyl)maleic anhydride was condensed with H2NCHMeCO2Et

to give I (R1-R3 = R6 = H, R4 = CHMeCO2Et, R5 = 3-indolyl).

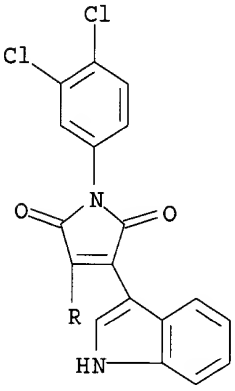
IT **137107-86-9P 137108-00-0P 137108-32-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiallergic and for immune disorders)

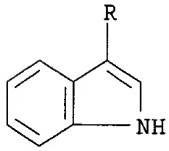
RN 137107-86-9 CAPLUS
CN 1H-Pyrrole-2,5-dione, 1-ethyl-3,4-di-1H-indol-3-yl- (9CI) (CA INDEX NAME)





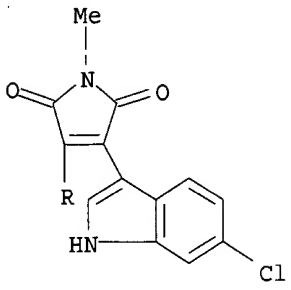
RN 137108-00-0 CAPLUS
CN 1H-Pyrrole-2,5-dione, 1-(3,4-dichlorophenyl)-3,4-di-1H-indol-3-yl- (9CI) (CA INDEX NAME)

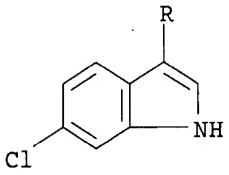




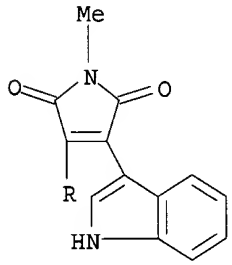
RN 137108-32-8 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-bis(6-chloro-1H-indol-3-yl)-1-methyl- (9CI) (CA

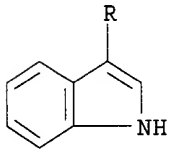
INDEX NAME)





IT **113963-68-1**, 1-Methyl-3,4-bis(3-indolyl)maleimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of antiallergics and compds. for immune disorders)
RN 113963-68-1 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





L3 ANSWER 70 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:228726 CAPLUS
DOCUMENT NUMBER: 114:228726
TITLE: Preparation of 3,4-bis(indol-3-yl)maleimides as protein kinase C inhibitors

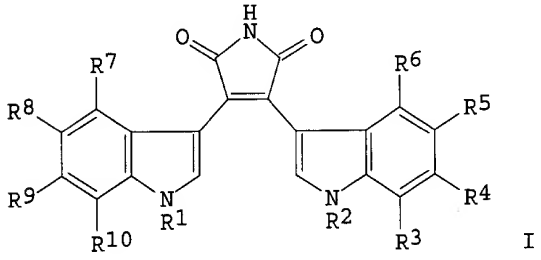
09622815

INVENTOR(S): Barth, Hubert; Hartenstein, Johannes; Rudolph, Claus; Schaechtele, Christoph; Betche, Hans Juergen; Osswald, Hartmut; Reck, Reinhard
PATENT ASSIGNEE(S): Goedecke A.-G., Germany
SOURCE: Eur. Pat. Appl., 69 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 397060	A2	19901114	EP 1990-108468	19900504
EP 397060	A3	19920102		
EP 397060	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 3914764	A1	19901108	DE 1989-3914764	19890505
DE 3942991	A1	19910704	DE 1989-3942991	19891227

PRIORITY APPLN. INFO.: DE 1989-3914764 A 19890505
DE 1989-3942991 A 19891227

OTHER SOURCE(S): CASREACT 114:228726; MARPAT 114:228726
GI



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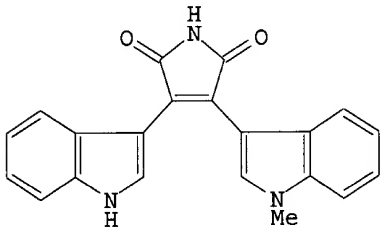
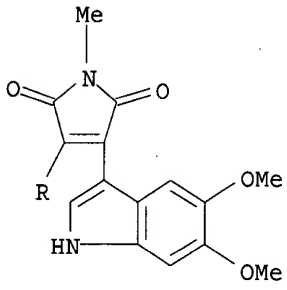


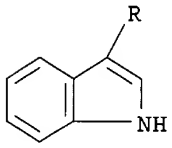
II

AB The title compds. [I; R1, R2 = H, alkyl, (substituted) PhCH2, aminoalkyl, heterocyclylalkyl, amidinothioalkyl, nitroguanidinoalkyl, isothiocyanatoalkyl, epoxyalkyl, alkoxycarbonylalkyl, carbamoylmethyl, etc.; R4-R10 = H, alkyl, alkoxy, acyloxy, halo, NO2, (substituted) amino, PhCH2O, OH, aminoalkoxy, heterocyclylalkoxy, CF3; 2 adjacent R4-R10 = OCH2O] were prepd. as antithrombotics, antiarteriosclerotics, antihypertensives, antinflammatories, allergy inhibitors, neoplasm inhibitors, virucides, immunomodulators, and CNS agents. Thus, indole was stirred 1 h with EtMgBr in THF at room temp.; 2-bromo-3-(1-methyl-1H-indol-3-yl)-N-methylmaleimide was added and the mixt. was refluxed 4 h to give

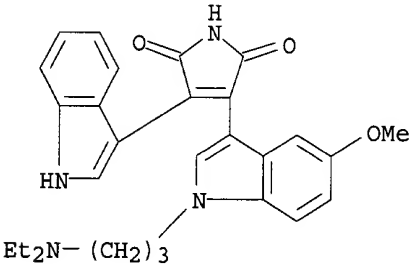
45% coupling product, which was refluxed with KOH in MeOH to give 79% maleic anhydride deriv. This was heated at 140.degree. with NH4OAc to give 83% title compd. II. II inhibited protein kinase C with an IC50 of 0.14 .mu.M, vs. 77 .mu.M against A kinase.

IT **133053-53-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for protein kinase C inhibitor)
RN 133053-53-9 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-(5,6-dimethoxy-1H-indol-3-yl)-4-(1H-indol-3-yl)-1-methyl- (9CI) (CA INDEX NAME)



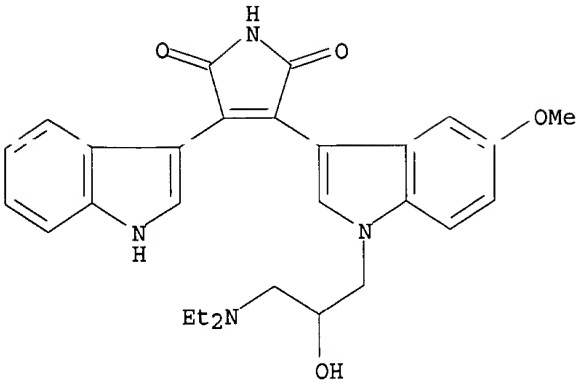


IT **133053-30-2P 133076-00-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as protein kinase C inhibitor)
RN 133053-30-2 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-[1-[3-(diethylamino)propyl]-5-methoxy-1H-indol-3-yl]-4-(1H-indol-3-yl)- (9CI) (CA INDEX NAME)



RN 133076-00-3 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-(1H-indol-3-yl)-4-[1-[3-(diethylamino)-2-hydroxypropyl]-5-methoxy-1H-indol-3-yl]-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



L3 ANSWER 71 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:185264 CAPLUS
DOCUMENT NUMBER: 114:185264
TITLE: Preparation of bis(indolyl)maleimides as protein kinase C inhibitors
INVENTOR(S): Barth, Hubert; Hartenstein, Johannes; Betche, Hans Juergen; Schaechtele, Christoph; Rudolph, Claus; Osswald, Hartmut
PATENT ASSIGNEE(S): Goedecke A.-G., Germany
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

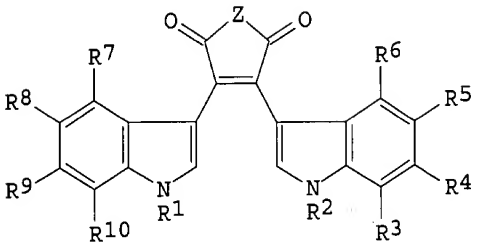
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3914764	A1	19901108	DE 1989-3914764	19890505
CA 2015996	AA	19901105	CA 1990-2015996	19900503
CA 2015996	C	20010828		
NO 9001989	A	19901106	NO 1990-1989	19900504
NO 179748	B	19960902		
NO 179748	C	19961211		
AU 9054666	A1	19901108	AU 1990-54666	19900504
AU 634541	B2	19930225		
EP 397060	A2	19901114	EP 1990-108468	19900504
EP 397060	A3	19920102		
EP 397060	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 53902	A2	19901228	HU 1990-2681	19900504
HU 207727	B	19930528		
ZA 9003409	A	19910227	ZA 1990-3409	19900504
DD 297970	A5	19920130	DD 1990-340398	19900504
AT 209202	E	20011215	AT 1990-108468	19900504
ES 2169719	T3	20020716	ES 1990-108468	19900504
JP 02306974	A2	19901220	JP 1990-115916	19900507
JP 2983248	B2	19991129		
US 5380746	A	19950110	US 1993-28528	19930309
US 5516915	A	19960514	US 1994-304740	19940912

PRIORITY APPLN. INFO.: DE 1989-3914764 A 19890505
DE 1989-3942991 A 19891227

US 1990-515795 B2 19900427
US 1991-715064 B1 19910611
US 1993-28528 A3 19930309

OTHER SOURCE(S): MARPAT 114:185264

GI



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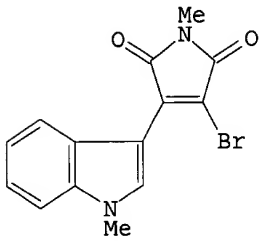


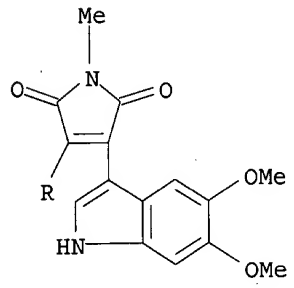
II

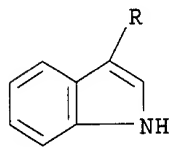
AB The title compds. [I; R1,R2 = H, (un)substituted alkyl, PhCH2, etc.; R3-R10 = H, alkyl, alkoxy, halo, etc.; Z = NH] were prepd. Thus, indole was stirred 1 h with EtMgBr in PhMe after which dibromomaleimide was added and the whole maintained 30 h at reflux to give, after N-methylation, indolylmaleimide II which was arylated in the same manner as previously to give, after hydrolysis, I (R1 = Me; R2-R10 = H) (III; Z = O). The latter was heated 30 min at 140.degree. with NH4OAc to give III (Z = NH) which had IC50 of 0.14 .mu.mol/L against protein kinase C in vitro.

IT **133053-53-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of protein kinase C inhibitors)

RN 133053-53-9 CAPLUS

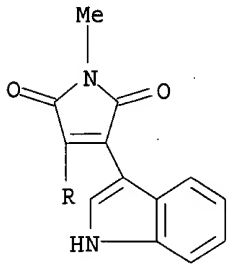
CN 1H-Pyrrole-2,5-dione, 3-(5,6-dimethoxy-1H-indol-3-yl)-4-(1H-indol-3-yl)-1-methyl- (9CI) (CA INDEX NAME)

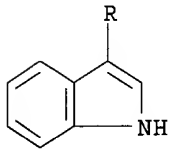




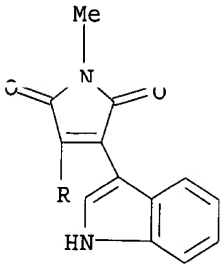
IT **113963-68-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of protein kinase C inhibitors)

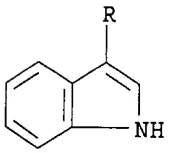
RN 113963-68-1 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





L3 ANSWER 72 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:4723 CAPLUS
DOCUMENT NUMBER: 114:4723
TITLE: The effect of new potent selective inhibitors of protein kinase C on the neutrophil respiratory burst
AUTHOR(S): Twomey, B.; Muid, R. E.; Nixon, J. S.; Sedgwick, A. D.; Wilkinson, S. E.; Dale, M. M.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Coll. London, London, WC1E 6BT, UK
SOURCE: Biochemical and Biophysical Research Communications (1990), 171(3), 1087-92
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New potent inhibitors of protein kinase C were found to inhibit protein kinase C isolated from rat brain and human neutrophils, with a large degree of selectivity over cAMP-dependent kinase and Ca2+/calmodulin-dependent kinase. These novel compds. were potent inhibitors of the fluoride, diC8- and formyl-methionyl-leucyl-phenylalanine-mediated respiratory bursts in intact neutrophils. The opsonized zymosan-stimulated burst was only marginally affected by the compds. These results differ from those obtained in studies with H7 and CI, (which are less potent and less specific protein kinase C inhibitors) and are consistent with the hypothesis that protein kinase C has a role in the transduction mechanism for the neutrophil oxidative burst stimulated with fluoride, formyl-methionyl-leucyl-phenylalanine and diC8.
IT **113963-68-1**, Ro 31-6045
RL: BIOL (Biological study)
(protein kinase C inhibition by, in neutrophil oxidative burst induction)
RN 113963-68-1 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





L3 ANSWER 73 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:98378 CAPLUS
DOCUMENT NUMBER: 112:98378
TITLE: Preparation of 3-(3-indolyl)pyrrole-2,5-diones and analogs as protein kinase inhibitors
INVENTOR(S): Davis, Peter David; Hill, Christopher Huw; Lawton, Geoffrey
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

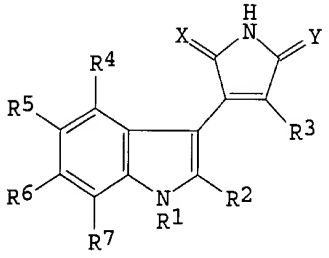
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 328026	A1	19890816	EP 1989-102025	19890206
EP 328026	B1	19930428		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8900865	A	19891025	ZA 1989-865	19890203
CZ 280738	B6	19960417	CZ 1989-752	19890203
SK 278989	B6	19980506	SK 1989-752	19890203
AU 8929658	A1	19890810	AU 1989-29658	19890206
AU 623630	B2	19920521		
HU 49348	A2	19890928	HU 1989-554	19890206
HU 201054	B	19900928		
US 5057614	A	19911015	US 1989-307104	19890206
AT 88704	E	19930515	AT 1989-102025	19890206
CA 1320194	A1	19930713	CA 1989-590178	19890206
ES 2054890	T3	19940816	ES 1989-102025	19890206
DK 8900558	A	19890811	DK 1989-558	19890207
DK 171891	B1	19970804		
JP 01233281	A2	19890919	JP 1989-27741	19890208
JP 07030071	B4	19950405		
NO 8900568	A	19890811	NO 1989-568	19890209

NO 172540	B	19930426		
NO 172540	C	19930804		
SU 1799382	A3	19930228	SU 1989-4613492	19890209
FI 8900652	A	19890811	FI 1989-652	19890210
FI 96861	B	19960531		
FI 96861	C	19960910		
US 36736	E	20000613	US 1998-14198	19980127

PRIORITY APPLN. INFO.:

GB 1988-3048	A	19880210
GB 1988-27565	A	19881125
EP 1989-102025	A	19890206
US 1989-307104	A5	19890206

GI



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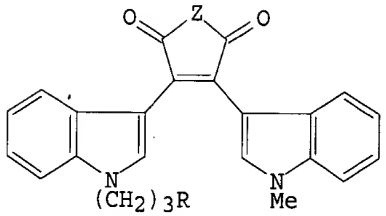


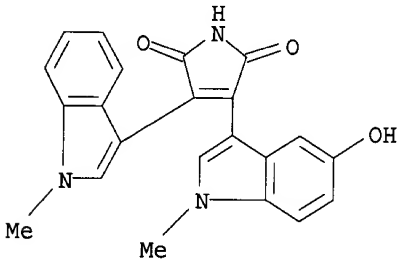
II

AB The title compds. (I; R1, R2 = H, alkyl, aryl, etc.; R3 = aryl, heteroaryl; R4-R7 = H, halo, alkyl, alkoxy, etc.; 1 of X, Y = O and the other = O, S, H and OH, H and H) were prepd. Thus, 1-(3-bromopropyl)indole (prepn. given) was stirred 2 h with (COCl)2 in CH2Cl2 and the product stirred 3 h with 1-methyl-3-indolylacetic acid in CH2Cl2 contg. (Me2CH)2NEt to give bis(indolyl)furandione II (R = Br, Z = O) which was converted in 3 steps to II (R = NH2, Z = NH). The latter was stirred 16 h with 1,1'-thiocarbonyldiimidazole in THF to give II (R = NCS, Z = NH) which had IC50 of 0.008 .mu.M for inhibition of protein kinase C in vitro.

IT **125313-48-6P 125313-63-5P 125314-73-0P**
125314-79-6P 125315-07-3P 125315-09-5P
125334-45-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as protein kinase inhibitor)

RN 125313-48-6 CAPLUS

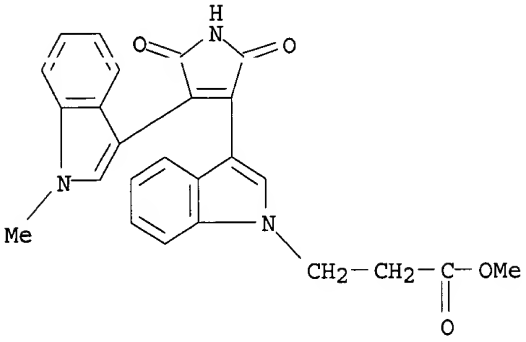
CN 1H-Pyrrole-2,5-dione, 3-(5-hydroxy-1-methyl-1H-indol-3-yl)-4-(1-methyl-1H-indol-3-yl)- (9CI) (CA INDEX NAME)



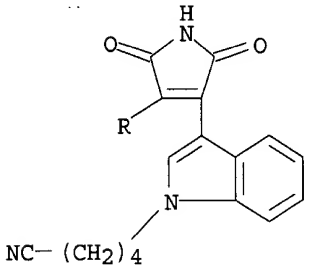
RN 125313-63-5 CAPLUS

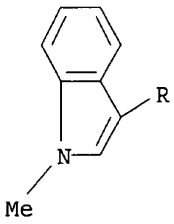
CN 1H-Indole-1-propanoic acid, 3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-

dioxo-1H-pyrrol-3-yl]-, methyl ester (9CI) (CA INDEX NAME)

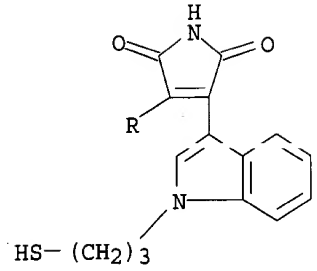


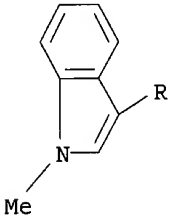
RN 125314-73-0 CAPLUS
CN 1H-Indole-1-pentanenitrile, 3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]- (9CI) (CA INDEX NAME)



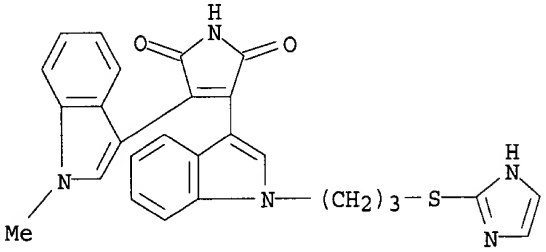


RN 125314-79-6 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-[1-(3-mercaptopropyl)-1H-indol-3-yl]-4-(1-methyl-1H-indol-3-yl)- (9CI) (CA INDEX NAME)

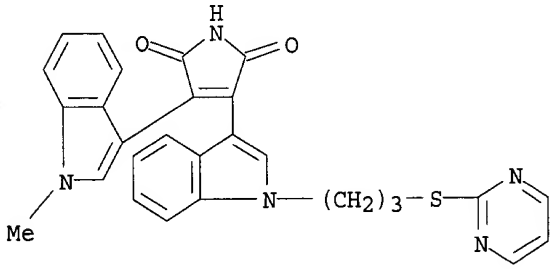




RN 125315-07-3 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-[1-[3-(1H-imidazol-2-ylthio)propyl]-1H-indol-3-yl]-4-(1-methyl-1H-indol-3-yl)- (9CI) (CA INDEX NAME)

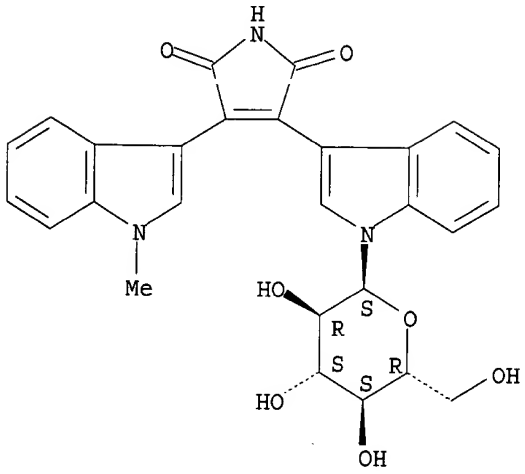


RN 125315-09-5 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-(1-methyl-1H-indol-3-yl)-4-[1-[3-(2-pyrimidinylthio)propyl]-1H-indol-3-yl]- (9CI) (CA INDEX NAME)

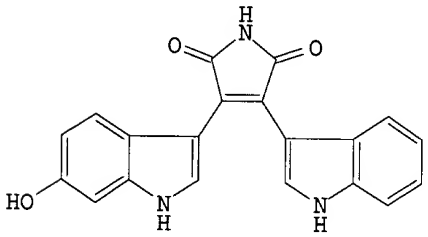


RN 125334-45-4 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-(1-.alpha.-D-glucopyranosyl-1H-indol-3-yl)-4-(1-methyl-1H-indol-3-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 74 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:94799 CAPLUS
DOCUMENT NUMBER: 110:94799
TITLE: Pigments of fungi, 57. Synthesis of arcyriarubin B and related bisindolylmaleimides
AUTHOR(S): Brenner, Michael; Rexhausen, Hans; Steffan, Bert; Steglich, Wolfgang
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Univ. Bonn, Bonn, D-5300, Fed. Rep. Ger.
SOURCE: Tetrahedron (1988), 44(10), 2887-92
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:94799
GI

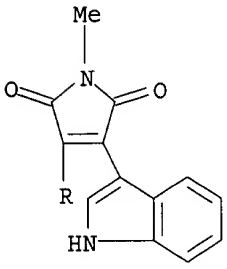


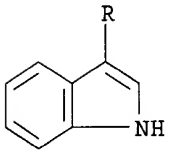
I

AB The reaction of 3-indolylmagnesium bromide with 2,3-dibromo-N-methylmaleimide in PhMe leads to 2,3-bis(indol-3-yl)-N-methylmaleimides. In THF a monosubstitution product is obtained which, after protection of the indole NH-group, was used to prep. unsym. substituted bisindolylmaleimides, including arcyriarubin B (I).

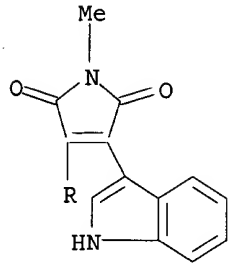
IT **113963-68-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

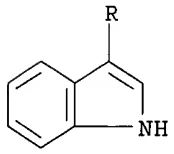
(prepn. and hydrolysis of)
RN 113963-68-1 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





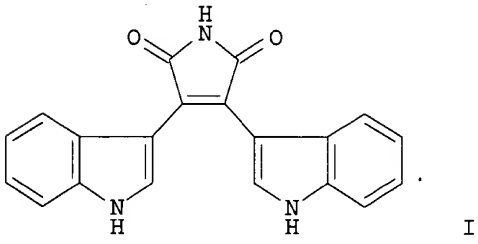
L3 ANSWER 75 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:204858 CAPLUS
DOCUMENT NUMBER: 108:204858
TITLE: Carbon-13 NMR spectroscopy of indole derivatives
AUTHOR(S): Morales-Rios, M. S.; Espineira, J.; Joseph-Nathan, P.
CORPORATE SOURCE: Cent. Invest. Estud. Avanzados, Inst. Politec. Nac., Mexico City, 07000, Mex.
SOURCE: Magnetic Resonance in Chemistry (1987), 25(5), 377-95
CODEN: MRCHEG; ISSN: 0749-1581
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The chem. shifts of 298 naturally occurring and synthetic compds. contg. the indole chromophoric group are listed. Substituent effects on 13C chem. shifts (SCS) induced by substitution on the heteroarom. five-membered ring are discussed. The data provide a ref. set for future 13C NMR investigations and highlight the need for unambiguous exptl. evidence to resolve controversial assignments for differently substituted representative indole derivs. Many original assignments have been changed, and values not considered to be unambiguously assigned are delineated. The 1J(CH) values for the parent indole were measured.
IT **113963-68-1**, 1-Methyl-3,4-bis(indole-3-yl)maleimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(carbon-13 NMR chem. shifts of)
RN 113963-68-1 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





=> d l3 55-64 ibib abs hitstr

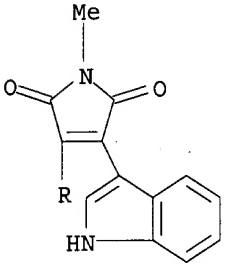
L3 ANSWER 55 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:29554 CAPLUS
DOCUMENT NUMBER: 124:232105
TITLE: A general approach to the synthesis of bisindolylmaleimides: synthesis of staurosporine aglycon
AUTHOR(S): Faul, Margaret M.; Sullivan, Kevin A.; Winneroski, Leonard L.
CORPORATE SOURCE: Chem. Process Res. Dev., Eli Lilly & Co., Indianapolis, IN, 46285-4813, USA
SOURCE: Synthesis (1995), (12), 1511-16
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Thieme
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:232105
GI

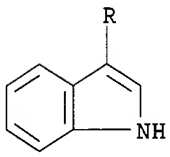


I

AB Bisindolylmaleimides were prepd. in 65-95% yield by reaction of an indole Grignard with either 2,3-dichloro-N-methylmaleimide or 2,3-dichloromaleimide. A 1-step synthesis of arcyriarubin A I in 72% yield affords ready access to the staurosporine aglycon.

IT **113963-68-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bisindolylmaleimides and of arcyriarubin A as staurosporine aglycon precursor)
RN 113963-68-1 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)

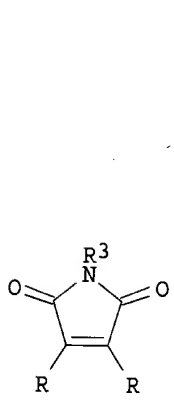




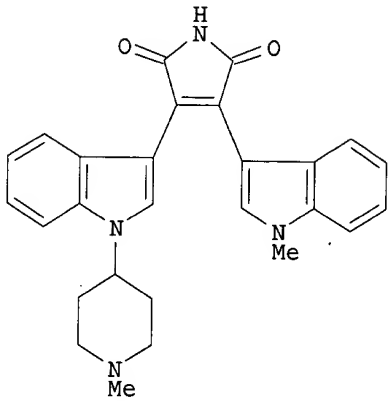
L3 ANSWER 56 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:921902 CAPLUS
DOCUMENT NUMBER: 123:339732
TITLE: Preparation of bis(indolyl)pyrrolediones as protein kinase C inhibitors
INVENTOR(S): Heath, William Francis Heath, Jr.; McDonald, John Hampton III; Paal, Michael; Ruether, Gerd; Schotten, Theo; Stenzel, Wolfgang
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9517182	A1	19950629	WO 1994-US14313	19941214
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5545636	A	19960813	US 1994-324948	19941018
AU 9513398	A1	19950710	AU 1995-13398	19941214
JP 09507066	T2	19970715	JP 1994-517479	19941214
EP 817627	A1	19980114	EP 1995-904892	19941214

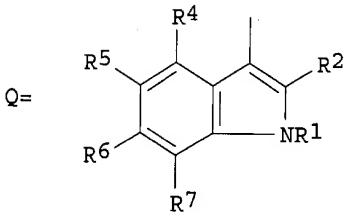
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT
PRIORITY APPLN. INFO.: US 1993-173741 19931223
US 1994-324948 19941018
WO 1994-US14313 19941214
OTHER SOURCE(S): MARPAT 123:339732
GI



I



II

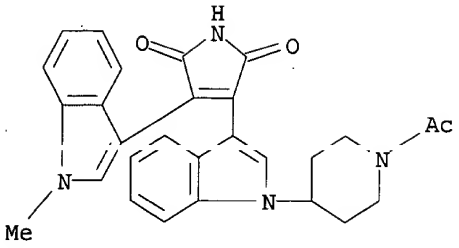


AB Title compds. [I; R = indolyl group Q; R1 independently = H, (un)substituted alkyl, heterocyclyl(alkyl), etc.; R2 independently = H, alkyl(thio), CF3, etc.; 1 pair of R1R2 = (CH2)XCH2; R3 = H, Ac; R4-R7 independently = H, halo, alkyl, alkoxy, etc.; X = (un)substituted alkylene, (alkyl)imino, etc.; r = 1-3] were prepd. Thus, 1-(1-methyl-4-piperidinyl)-1H-indole (prepn. given) was cyclocondensed with iso-Pr 1-methyl-3-indolylacetimidate to give title compd. II which had IC50 of 0.02 and 0.01.mu.M against .beta.1 and .beta.2 isoenzymes of protein kinase C, resp.

IT **170364-46-2P 170364-69-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bis(indolyl)pyrrolediones as protein kinase C inhibitors)

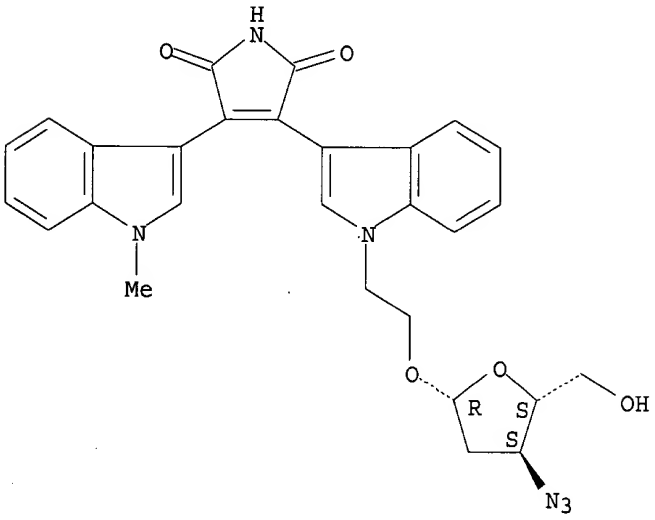
RN 170364-46-2 CAPLUS

CN Piperidine, 1-acetyl-4-[3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]- (9CI) (CA INDEX NAME)



RN 170364-69-9 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-[1-[2-[(3-azido-2,3-dideoxy-.beta.-D-erythro-pentofuranosyl)oxy]ethyl]-1H-indol-3-yl]-4-(1-methyl-1H-indol-3-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 57 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:916432 CAPLUS
DOCUMENT NUMBER: 123:314034
TITLE: Improved synthesis of bisindolylmaleimides.
INVENTOR(S): Faul, Margaret Mary; Heath, William Francis, Jr.; Jirousek, Michael Robert; Mcdonald, John Hampton, III; Rito, Christopher John; Winneroski, Leonard Larry, Jr.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 657411	A1	19950614	EP 1994-308948	19941202
EP 657411	B1	19990609		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE

US 5541347	A	19960730	US 1994-317140		19941003
US 5698578	A	19971216	US 1996-734292		19961021
PRIORITY APPLN. INFO.:			US 1993-163060	A	19931207
			US 1994-317140	A	19941003
			US 1994-316973	B2	19941003
			US 1995-457060	A1	19950601

OTHER SOURCE(S): CASREACT 123:314034; MARPAT 123:314034
GI

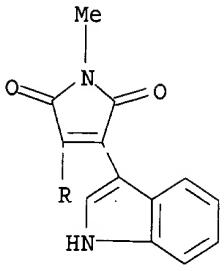
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

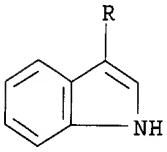
AB The invention provides a novel synthesis of macrocyclic title compds. I [Z = (CH2)n; R = H, halo, alkyl, OH, alkoxy, haloalkyl, NO2, NR5R6, alkanoylamino; R1 = alkyl, alkoxy, OH, CO2H, cyano, SH, (un)substituted NH2, etc.; m = 0-3; n = 1-3], which are known antagonists of protein kinase C (PKC). The compds. are produced in high yield and without expensive chromatog. sepns. via the novel linking-group intermediates II [R2 = N3, protected NH2 or protected OH; L1 = leaving groups; Z = (CH2)n; n = 1-3]. The synthesis is particularly advantageous because it is stereoselective. For example, (S)-O-tritylglycidol reacted with vinylmagnesium bromide and CuI to give 96% (S)-CH2:CHCH2CH(OH)CH2OCPh3, which reacted with NaH and allyl bromide to give 98% diolefin (S)-CH2:CHCH2CH(CH2OCPh3)OCH2CH:CH2. This underwent ozonolysis and redn. with NaBH4 to give 100% diol, which was converted to 88% key intermediate (S)-II [ZR2 = CH2OCPh3, L1 = MeSO3, n = 1]. This underwent cyclization with 2,3-bis(1H-indol-3-yl)-N-methylmaleimide in DMF contg. Cs2CO3 under high-diln. conditions to give 57% cyclized product III, which was converted in 5 steps to target compd. (S)-I [R = H, m = 0, n = 1, ZR1 = CH2NMe2].

IT **113963-68-1P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; improved prepn. of bisindolylmaleimides)

RN 113963-68-1 CAPLUS

CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





L3 ANSWER 58 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:902566 CAPLUS
DOCUMENT NUMBER: 123:314033
TITLE: Preparation of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors.
INVENTOR(S): Heath, William Francis, Jr.; Jirousek, Michael Robert; Mcdonald, John Hampton, III; Rito, Christopher John
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 657458	A1	19950614	EP 1994-308947	19941202
EP 657458	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2137203	AA	19950608	CA 1994-2137203	19941202
FI 9405706	A	19950608	FI 1994-5706	19941202
NO 9404643	A	19950608	NO 1994-4643	19941202
AU 9479188	A1	19950615	AU 1994-79188	19941202
AU 687909	B2	19980305		
BR 9404831	A	19950808	BR 1994-4831	19941202
JP 07215977	A2	19950815	JP 1994-299399	19941202
CN 1111247	A	19951108	CN 1994-119362	19941202
CN 1050844	B	20000329		
HU 71130	A2	19951128	HU 1994-3468	19941202
HU 219709	B	20010628		
RU 2147304	C1	20000410	RU 1994-42922	19941202
TW 425397	B	20010311	TW 1994-83111226	19941202
AT 204579	E	20010915	AT 1994-308947	19941202
PL 182124	B1	20011130	PL 1994-306084	19941202
ES 2162843	T3	20020116	ES 1994-308947	19941202
BR 9502611	A	19961001	BR 1995-2611	19950531

US 5698578	A	19971216	US 1996-734292	19961021
CN 1220266	A	19990623	CN 1997-126094	19971209
CN 1055089	B	20000802		
HK 1013827	A1	20020705	HK 1998-115199	19981223
FI 2000000516	A	20000307	FI 2000-516	20000307
FI 2001001109	A	20010528	FI 2001-1109	20010528

PRIORITY APPLN. INFO.: US 1993-163060 A 19931207
US 1994-316973 A 19941003
US 1995-457060 A1 19950601

OTHER SOURCE(S): MARPAT 123:314033

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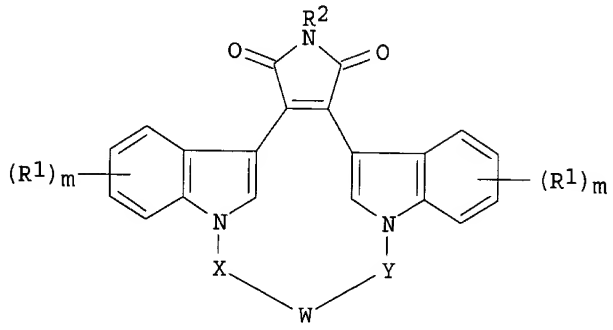

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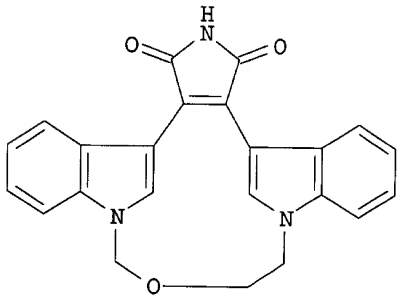


II

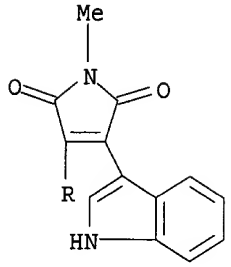
AB Title compds. [I; W = O, S, SO, SO2, CO, (substituted) alkylene, alkenylene, arylene, heterocyclylene, CONH, etc.; X, Y = (substituted) alkylene; XYW = (CH2)nA; A = amino acid residue; n = 2-5; R1 = H, halo, alkyl, OH, alkoxy, haloalkyl, NO2, amino, alkylcarbonylamino; R2 = H, Ac, NH2, OH; m = 0-3], were prepd. Thus, 3,4-bis(3'-indolyl)furan-2,5-dione in DMF was treated with NaH and then (BrCH2CH2)2O to give 20% cyclocondensation product, which in DMF was treated with hexamethyldisilazane in MeOH to give 72% title compd. (II). II inhibited protein kinase C .beta.-1 with IC50 = 0.05 .mu.M. I preferentially inhibit the .beta.-isoenzymes by a factor of .gtoreq.10 over other isoenzymes.

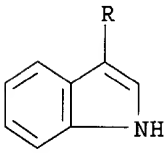
IT **113963-68-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors)

RN 113963-68-1 CAPLUS

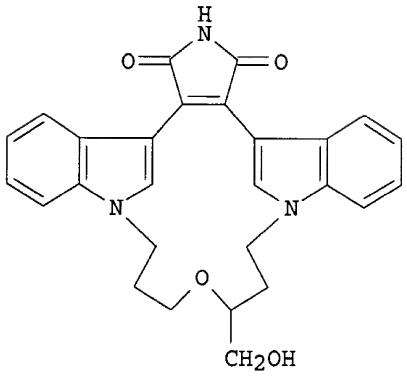
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX

NAME)





L3 ANSWER 59 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:827713 CAPLUS
DOCUMENT NUMBER: 124:29743
TITLE: Synthesis of bisindolylmaleimide macrocycles
AUTHOR(S): Jirousek, Michael R.; Gillig, James R.; Neel, David A.; Rito, Christopher J.; O'Bannon, Douglas; Heath, William F.; McDonald, John H., III; Faul, Margaret M.; Winneroski, Leonard L.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly Co., Indianapolis, IN, 46285, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1995), 5(18), 2093-6
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:29743
GI



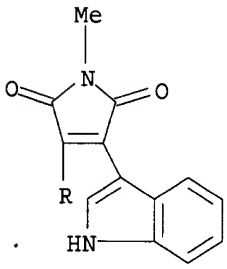
I

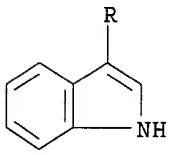
AB The synthesis of a novel class of N,N'-macrocyclic bisindolylmaleimides, e.g., I, is reported. The key step involves a remarkably efficient intramol. cyclization reaction. The method was further developed to provide an efficient synthesis of this type of macrocycle through an intermol. alkylation with subsequent intramol. cyclization.

IT **113963-68-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of bisindolylmaleimide macrocycles)

RN 113963-68-1 CAPLUS

CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





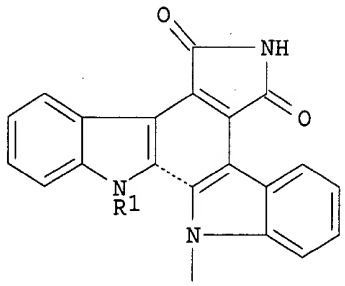
L3 ANSWER 60 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:315569 CAPLUS
DOCUMENT NUMBER: 122:106539
TITLE: Preparation of amino acid and peptide bis(indolyl)maleimide and indolopyrrolocarbazole derivatives as inhibitors of protein kinase C
INVENTOR(S): Trostmann, Uwe; Hartenstein, Johannes; Barth, Hubert; Reck, Reinhard; Schaechtele, Christoph; Rudolph, Klaus; Koelch, Walter
PATENT ASSIGNEE(S): Goedecke AG, Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4243321	A1	19940623	DE 1992-4243321	19921221
JP 2001061844	A2	20010313	JP 2000-237799	19920930
WO 9414798	A1	19940707	WO 1993-EP3611	19931220

W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9458137 A1 19940719 AU 1994-58137 19931220
EP 674632 A1 19951004 EP 1994-903834 19931220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 08504788 T2 19960521 JP 1993-514794 19931220
US 5750555 A 19980512 US 1996-464666 19961115
PRIORITY APPLN. INFO.: US 1992-840211 A 19920224
JP 1993-514794 A3 19920930
DE 1992-4243321 A 19921221
WO 1993-EP3611 W 19931220
OTHER SOURCE(S): MARPAT 122:106539
GI

Q1=



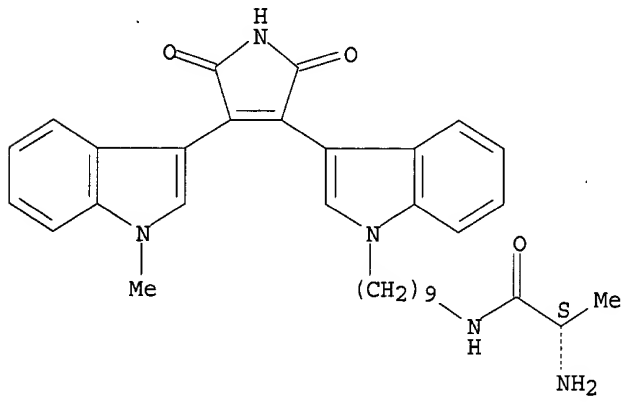
AB AXYEnR5 [A = residue Q1; R1, R2, R4 = H, alkyl; dotted line = optional bond; X = bond, alkylene; Y = bond, NR2, CO, CS, CH:CH, PO(OH)O, SO2; n = 1-20; E = NR2(CHR3)mCO; m = 1-6; R3 = H, amino acid side chain; R5 = H, amino, OR4], with provisos, were prepd. Thus, 2-[(1-methyl)-1H-indol-3-yl]-3-[1-(3-serylaminopropyl)-1H-indol-3-yl]maleimide, prepd. by soln. phase coupling methods, inhibited rat brain protein kinase C with IC50 = 14 nM.

IT **160531-98-6P 160532-04-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as protein kinase C inhibitor)

RN 160531-98-6 CAPLUS

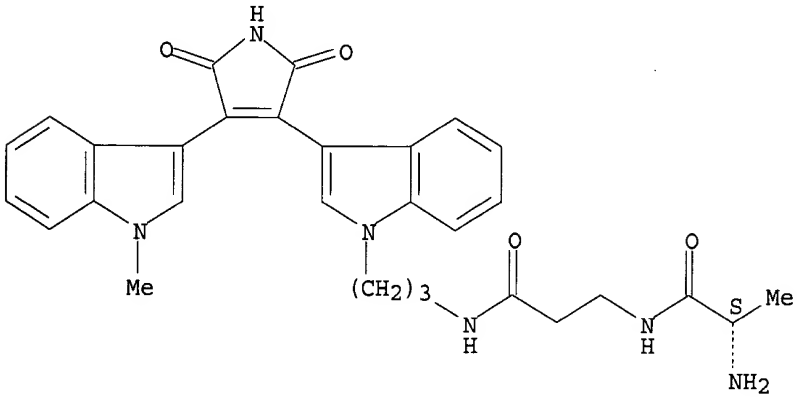
CN Propanamide, 2-amino-N-[9-[3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]nonyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 160532-04-7 CAPLUS
CN .beta.-Alaninamide, L-alanyl-N-[3-[3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

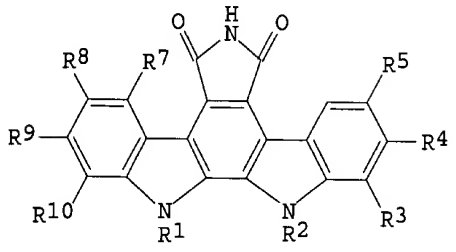


L3 ANSWER 61 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:270356 CAPLUS
DOCUMENT NUMBER: 120:270356
TITLE: Preparation of 5,7-dioxo-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazoles as protein kinase inhibitors useful as drugs
INVENTOR(S): Kleinschroth, Juergen; Hartenstein, Johannes; Schaechtele, Christoph; Rudolph, Claus; Barth, Hubert; Aranda, Julian; Betche, Hans Juergen
PATENT ASSIGNEE(S): Goedecke AG, Germany
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4217964	A1	19931202	DE 1992-4217964	19920530
WO 9324491	A1	19931209	WO 1993-EP1347	19930528
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9343194	A1	19931230	AU 1993-43194	19930528
AU 687350	B2	19980226		
EP 642513	A1	19950315	EP 1993-912820	19930528
EP 642513	B1	20000809		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07508268	T2	19950914	JP 1993-500204	19930528
HU 71102	A2	19951128	HU 1994-3419	19930528
RU 2126007	C1	19990210	RU 1994-46306	19930528
AT 195315	E	20000815	AT 1993-912820	19930528
ES 2152252	T3	20010201	ES 1993-912820	19930528

FI 9405625	A	19941129	FI 1994-5625		19941129
NO 9404564	A	19950130	NO 1994-4564		19941129
US 5883114	A	19990316	US 1995-343435		19950215
US 5945440	A	19990831	US 1998-74139		19980507
PRIORITY APPLN. INFO.:			DE 1992-4217964	A	19920530
			WO 1993-EP1347	A	19930529

OTHER SOURCE(S): MARPAT 120:270356
GI



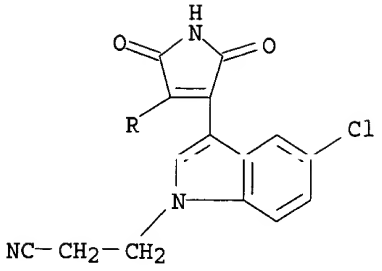
I

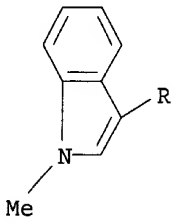
AB Title compds. I; R1, R2 = H, alkyl, alkenyl, alkynyl, epoxy, (substituted) aryl, aralkyl, cyano, cyanoalkyl, azidoalkyl, alkylthioalkyl, isocyanoalkyl, arylsulfonyloxyalkyl, carbamoylalkyl, etc.; R1R2 = (substituted) alkylene; R3-R10 = H, alkyl, alkoxy, alkylthio, benzyloxy, acyl, halo, nitro, OH, acyloxy, CF3, amino, haloalkyl, alkylsulfinyl, alkylsulfonyl, etc.; were prepd. Thus, 3-[1-(2-cyanoethyl)-5-methoxy-3-indolyl]-4-(1-methyl-3-indolyl)-1H-pyrrole-2,5-dione [prepn. from 1-(2-cyanoethyl)-5-methoxyindole and 1-methyl-3-indolylacetic acid given] was refluxed 30 min with 2,3-dichloro-5,6-dicyano-p-benzoquinone in PhMe to give 13-(2-cyanoethyl)-6,7,12,13-tetrahydro-3-methoxy-12-methyl-5,7-dioxo-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole. This inhibited myosin light chain kinase and protein kinase C with IC50 = 0.2 and 0.0015 .mu.M, resp. I also demonstrated antihypertensive, antitumor, and anti-HIV activities.

IT **153998-30-2P 153998-35-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and oxidative cyclization of, in prepn. of protein kinase inhibitor)

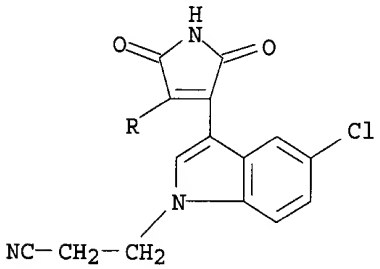
RN 153998-30-2 CAPLUS

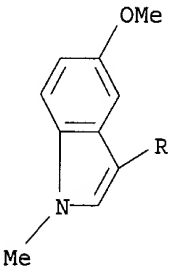
CN 1H-Indole-1-propanenitrile, 5-chloro-3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]- (9CI) (CA INDEX NAME)



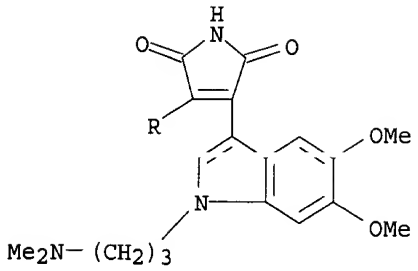


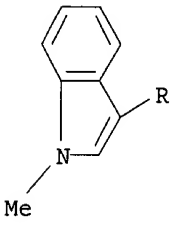
RN 153998-35-7 CAPLUS
CN 1H-Indole-1-propanenitrile, 5-chloro-3-[2,5-dihydro-4-(5-methoxy-1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]- (9CI) (CA INDEX NAME)



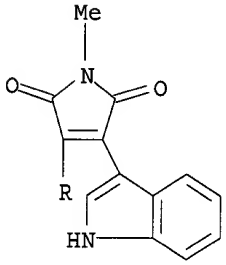


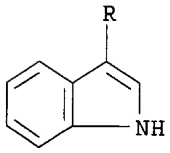
IT **153998-44-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for protein kinase inhibitor)
RN 153998-44-8 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3-[1-[3-(dimethylamino)propyl]-5,6-dimethoxy-1H-indol-3-yl]-4-(1-methyl-1H-indol-3-yl)- (9CI) (CA INDEX NAME)





IT **113963-68-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of protein kinase inhibitor)
RN 113963-68-1 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)





L3 ANSWER 62 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:182350 CAPLUS
DOCUMENT NUMBER: 120:182350
TITLE: Interactive multivariate analysis of bisindolylmaleimides as potent protein kinase C antagonists
AUTHOR(S): Mager, Peter P.
CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Univ. Leipzig, Leipzig,

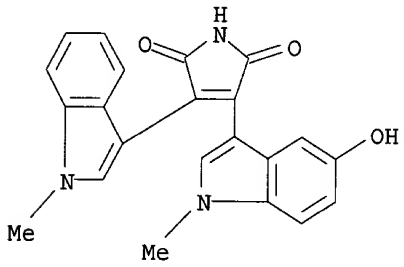
7010, Germany
SOURCE: Drug Design and Discovery (1993), 10(3), 231-48
CODEN: DDDIEV; ISSN: 1055-9612
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The isoenzyme protein kinase C (PKC) inhibitory activity of substituted bisindolylmaleimides depends on the mol. wt., the total charge, and dipole moments. The validity of the resulting QSAR equation was investigated by interactive diagnostic statistics and multivariate simultaneous statistical inference. Mol. mechanics and dynamics can be used to study possible reasons of flagged observations (high-leverage points, influential data, outliers) of QSAR systems.

IT **125313-48-6**
RL: BIOL (Biological study)
(protein kinase C inhibitory activity of, QSAR study of)

RN 125313-48-6 CAPLUS

CN 1H-Pyrrole-2,5-dione, 3-(5-hydroxy-1-methyl-1H-indol-3-yl)-4-(1-methyl-1H-indol-3-yl)- (9CI) (CA INDEX NAME)



L3 ANSWER 63 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:106798 CAPLUS
DOCUMENT NUMBER: 120:106798
TITLE: Indole derivatives with antiviral activity
INVENTOR(S): Slater, Martin John; Cockerill, George Stuart; Littler, Edward; Yeates, Clive Leonard
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

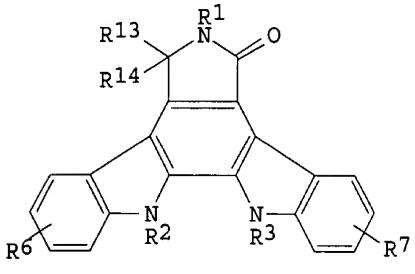
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9318766	A1	19930930	WO 1993-GB571	19930319
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9337614	A1	19931021	AU 1993-37614	19930319
AU 685389	B2	19980122		
EP 630242	A1	19941228	EP 1993-906709	19930319
EP 630242	B1	19990120		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

JP 07504674	T2	19950525	JP 1993-516379	19930319
AT 175873	E	19990215	AT 1993-906709	19930319
ES 2125976	T3	19990316	ES 1993-906709	19930319
US 5547976	A	19960820	US 1994-290921	19940823

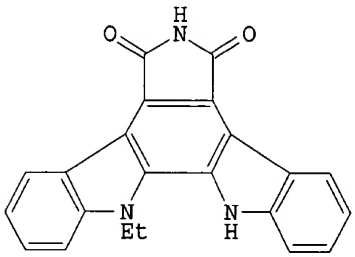
PRIORITY APPLN. INFO.: GB 1992-6056 19920320
GB 1992-6810 19920327
WO 1993-GB571 19930319

OTHER SOURCE(S): MARPAT 120:106798

GI



I



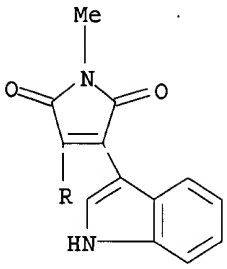
II

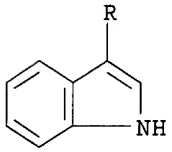
AB The use of the title compds., 5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole derivs. I (R1-R3 = hydrogen, acyl, alkyl, etc.; R6, R7 = hydrogen, alkyl, etc.; R13, R14 = hydrogen, alkoxy, etc.; R13R14 = oxygen) for the manuf. of pharmaceuticals for the treatment or prophylaxis of viral infections is claimed. Said viral infections are caused by herpes virus, retrovirus, hepatitis virus, coxsackie virus or hepatitis C virus. An example compd. is 12-ethyl-12,13-dihydro-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione (II).

IT **113963-68-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for indolo[2,3-a]pyrrolo[3,4-c]carbazole deriv. (virucide))

RN 113963-68-1 CAPLUS

CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)

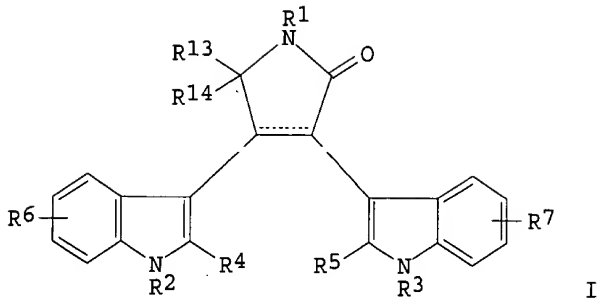




L3 ANSWER 64 OF 75 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:106760 CAPLUS
DOCUMENT NUMBER: 120:106760
TITLE: Antiviral bis(indolyl)pyrrolidones
INVENTOR(S): Slater, Martin John; Cockerill, George Stuart; Littler, Edward
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9318765	A1	19930930	WO 1993-GB570	19930319
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9337613	A1	19931021	AU 1993-37613	19930319
EP 630241	A1	19941228	EP 1993-906708	19930319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07504673	T2	19950525	JP 1993-516378	19930319

PRIORITY APPLN. INFO.: GB 1992-6056 19920320
GB 1992-6809 19920327
WO 1993-GB570 19930319
OTHER SOURCE(S): MARPAT 120:106760
GI



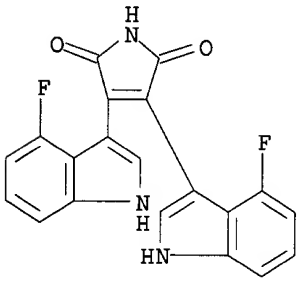
I

AB The title compds. I [R1 = H, alkylcarbonyl, arylcarbonyl, CO2H, carboxylate ester, (un)substituted C1-8 alkyl, (un)substituted C1-8 alkenyl, etc.; R2, R3 = H, arylcarbonyl, alkylcarbonyl, CHO, CO2H, carboxylate ester, H, etc.; R4, R5 = H, (un)substituted C1-6 alkyl, (un)substituted C3-7 cycloalkyl, (un)substituted aryl, etc.; R6, R7 = H, (un)substituted C1-6 alkyl, CN, NO2, halogen, methylenedioxy etc.; R13, R14 = H, alkoxy, aryloxy, alkylthio, arylthio, etc.; R13R14 = :O], useful in the treatment of coxsackie virus, (no data), varicella zoster virus (no data), Epstein-Barr virus (no data), cytomegalovirus, etc., are prepd. and I-contg. formulations presented. Thus, 3,4-bis(1H-2-methylindol-3-yl)-2,5-dihydro-1-phenylmethyl-1H-pyrrolo-2,5-dione was reacted in EtOH with Zn amalgam, producing cis-3,4-bis(2-methyl-1H-indol-3-yl)-1-phenylmethylsuccinimide (II). II demonstrated 50% viral inhibitory concn. against human cytomegalovirus-infected MRC5 (human embryonic lung) cells of 8.5 .mu.M.

IT **152538-02-8P 152538-12-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antiviral activity of)

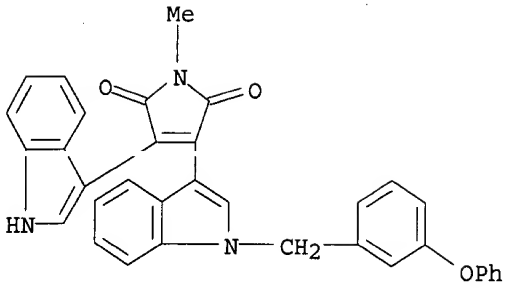
RN 152538-02-8 CAPLUS

CN 1H-Pyrrole-2,5-dione, 3,4-bis(4-fluoro-1H-indol-3-yl)- (9CI) (CA INDEX NAME)



RN 152538-12-0 CAPLUS

CN 1H-Pyrrole-2,5-dione, 3-(1H-indol-3-yl)-1-methyl-4-[1-[(3-phenoxyphenyl)methyl]-1H-indol-3-yl]- (9CI) (CA INDEX NAME)



IT **113963-68-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antiviral activity of, reaction of)
RN 113963-68-1 CAPLUS
CN 1H-Pyrrole-2,5-dione, 3,4-di-1H-indol-3-yl-1-methyl- (9CI) (CA INDEX NAME)